REMARKS

Status of the Claims

Pending claims

Claims 1 to 92 as filed are pending.

The Restriction Requirement

The Patent Office alleged that the pending claims of the application are directed to nine separate and distinct inventions under 35 U.S.C. §121, and requested an election of a sequence of SEQ ID NOs:19-54 for each of Groups I to IX.

Group I: Claims 1-23, 40, 41, 67-85, drawn to an isolated nucleic acid encoding a polypeptide having phosphatase activity, methods of expressing said nucleic acid, oligonucleotide probes.

Group II: Claims 24-35, 64, 86, 87, drawn to an isolated polypeptide having phosphatase activity and enzyme preparations comprising said polypeptide.

Group III: Claims 36-39, drawn to an antibody that binds to a phosphatase.

Group IV: Claims 42-55, drawn to a method of generating a variant.

Group V: Claims 56-60, drawn to a computer readable medium and a computer system comprising a nucleic acid sequence.

Group VI: Claims 61-63, drawn to a method for comparing a first sequence to a reference sequence or identifying a feature in a sequence.

Group VII: Claim 65, drawn to a method for catalyzing the hydrolysis of phosphates.

Group VIII: Claim 66 drawn to an assay for identifying functional polypeptide fragments.

Group IX: Claims 88-92, drawn to a method for modifying small molecules.

In response to the restriction requirement, Applicants elected, with traverse, Group I, claims 1-23, 40, 41, 67- 81, and 82-85, as pertaining to SEQ ID NO:21 and SEQ ID NO:30, drawn to isolated nucleic acids encoding a polypeptide having phosphatase activity, methods of expressing said nucleic acids, and oligonucleotide probes.

In their traversal to the restriction requirement Applicants requested that the Patent Office reconsider and join (nucleic acid/amino acid sequences) SEQ ID NOS:21, 30; 22, 31; 23, 32; 26, 35; and 45, 46 for Group I. Applicants set forth distinct and specific errors in the

restriction requirement and reasons for the Patent Office to reconsider and withdraw, in part, the restriction requirement. Accordingly, Applicants have preserved their right to petition the restriction to the Group Director under 37 CFR §1.144; see also MPEP §818.03(c); pg 800-60, 8th Edition, August 2001.

Claims amended and added in the instant amendment

In the present response, claims 1 to 23, 40, 41, 67 to 77 and 79 to 85 are amended, new claims 93 to 108 added, and claims 24 to 39, 42 to 66 and 86 to 92 are canceled without prejudice. Accordingly, after entry of the instant amendment, claims 1 to 23, 40, 41, 65 to 85 and 93 to 108 are pending and under examination.

Outstanding Rejections

Claims 2, 3 to 5, 6 to 14, 15, 17 to 21, 67 to 81 and 82 to 84 are rejected under 35 U.S.C. §112, second paragraph. Claims 3 to 23, 40, 41, 67 to 81 and 82 to 85 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors at the time the application was filed had possession of the claimed invention. Claims 1 to 23, 40, 41, 67 to 81 and 82 to 85 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled by the specification. Claims 4 to 21, 67 to 70, 79 and 85 are rejected under 35 U.S.C. §102(e) for allegedly being anticipated by U.S. Patent No. 5,792,903, Hirschberg, et al., filed March 7, 1995, a continuation-in-part of USSN 08/142,195, filed on Oct. 25, 1993 (hereinafter "Hirschberg"). Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

Support for the Claim Amendments

Support for the claim amendments can be found throughout the specification. For example, support for claimed directed to nucleic acids defined by, inter alia, their ability to hybridize to an exemplary nucleic acid under various hybridization conditions can be found, inter alia, in paragraphs 168 to 179, pages 40 to 42, of the specification. Accordingly, Applicants respectfully submit that no new matter is introduced by the instant amendments.

Informalities in the specification

The disclosure is objected to for various informalities:

A typographical error on page 7, paragraph 36. The instant amendment addresses this issue.

Page 73 (lacking a page number) has been replaced with a new page 73 (including the page number).

The specification has been amended to comply with 37 C.F.R. 1.821(a)(1), and rule 821 per MPEP 2422.02.

Claim Objections

Claims 1 to 23, 40, 41 and 67 to 85 have been amended to only be directed to elected subject matter.

Claim 85 has been amended as suggested in the Office Action.

Issues under 35 U.S.C. §112, second paragraph

Claims 2, 3 to 5, 6 to 14, 15, 17 to 21, 67 to 81 and 82 to 84 are rejected under 35 U.S.C. §112, second paragraph.

The phrase "sequences substantially identical thereto"

The Patent Office alleges that the phrase "sequences substantially identical thereto" makes claim 2 broader than claim 1. The instant amendment addresses this issue.

The terms "high stringency," "moderate stringency" and "low stringency"

The Patent Office alleges that the terms "high stringency,""moderate stringency" and "low stringency" make the claims indefinite because the specification does not define what constitutes "stringent." The instant amendment addresses this issue.

The term "sequence comparison algorithm"

The issue of antecedent basis for the term "sequence comparison algorithm" in claim 15 is addressed by the instant amendment.

The phrase "sequences substantially identical thereto"

The Patent Office alleges that the phrase "sequences substantially identical thereto" makes claim 16 indefinite. The instant amendment addresses this issue.

Claims 17 to 21

The Patent Office alleged that claims 17 to 21 are indefinite. The instant amendment addresses this issue.

The terms "homology" and "percent identity"

The Patent Office alleges that inconsistent use of the terms "homology" and "percent identity" make claims 6 to 14 and 17 to 21 indefinite. The instant amendment addresses this issue.

Issues under 35 U.S.C. §112, first paragraph

Written Description

Claims 3 to 23, 40, 41, 67 to 81 and 82 to 85 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors at the time the application was filed had possession of the claimed invention.

The Patent Office alleges, inter alia, that because the specification provides a single representative species and there is no disclosure of any particular structure/ function relationship in the single disclosed species, the genus of claimed nucleic acids is not sufficiently described in the specification under the written description requirement of section 112, first paragraph.

Applicants respectfully submit that the claimed invention is sufficiently described in the specification so that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing.

Applicants respectfully refer to the USPTO guidelines concerning compliance with the written description requirement of U.S.C. §112, first paragraph. In example 14 of the guidelines (a copy of which is attached as Exhibit G), a claim reciting variants claimed by sequence identity to a sequence is sought (specifically, "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B). In the example, the specification is described as providing SEQ ID NO:3 and a function for the protein. The specification contemplates, but does not exemplify variants of SEQ ID NO:3

that can have substitutions, deletions, insertions and additions. Procedures for making proteins with substitutions, deletions, insertions, and additions are routine in the art and an assay is described which will identify other proteins having the claimed catalytic activity. The analysis of example 14 states that procedures for making variants (which have 95% sequence identity) are conventional in the art. The Guidelines conclusion states that the disclosure meets the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention.

The USPTO guidelines recognize that the written description requirement is met for a genus of polypeptides described by structure, a physico-chemical property (e.g., a % sequence identity, stringent hybridization) and a defined function. Accordingly, the genus of claimed polypeptides also meet the written description requirements of section 112.

Analogously, the claimed nucleic acids are described by structure (the exemplary nucleic acid), a physico-chemical property (percent sequence identity or stringent hybridization) and function (phosphatase activity). All nucleic acids of the claimed genus must have at least about 50% sequence identity to SEQ ID NO:21, and complementary sequences thereof, or, must hybridize to a nucleic acid of claim 1 (a nucleic acid having at least about 50% sequence identity to SEQ ID NO:21) under conditions of defined stringency, e.g., high, moderate or low stringency.

Furthermore, the claims fully comply with the requirements for written description of a genus of nucleic acids as set forth in University of California v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed. Cir. 1997). In Lilly, the Court stated that, "[a] description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs....*or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.*" (emphasis added) Lilly, 43USPQ2d at 1406. As noted above, the instant claims clearly set forth specific structural and physical characteristics of the claimed hydrogenase-encoding nucleic acids. The claimed genus of polypeptides all must have a serine protease activity and a specific physical characteristic, e.g., a % sequence identity or stringent hybridization to the exemplary nucleic acid. Therefore, the claimed sequences are defined via shared physical and structural properties in terms that "convey with reasonable clarity to those

skilled in the art that Applicant, as of filing date sought, was in possession of invention." (Vas-Cath Inc. V. Mahukar, 19 USPQ2d 1111, (Fed Cir. 1991)).

More recently, the Federal Circuit stated

Similarly, in this court's most recent pronouncement, it noted:

> More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.

Amgen, 314 F.3d at 1332 [Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1330, 65 USPQ2d 1385, 1397 (Fed. Cir. 2003)].

Moba, B.V. v. Diamond Automation, Inc., 2003 U.S. App. LEXIS 6285; Fed. Cir. 01-1063, -1083, April 1, 2003.

Analogously, the disclosed function of the serine proteases encoded by the claimed nucleic acids of the instant invention is sufficiently correlated to a particular, known structure (the exemplary sequences) and a physical (physico-chemical) property (percent sequence identity or stringent hybridization). Accordingly, the claimed sequences are defined via shared physical and structural properties (and function - phosphatase activity) in terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention.

Applicants also respectfully note that claims directed to a genus of polypeptide-encoding nucleic acids as described and enabled by the specific physical characteristic of percent sequence identity or stringent hybridization and function have been issuing from the USPTO recently and for many years, see, e.g., U.S. Patent Nos. 6,541,684; 6,541,236; 6,541,220; 6,534,309; 6,492,150; 6,465,210; 6,413,522; 6,384,304; 6,342,657; 6,274,790 (selected claims from these patents are attached as Exhibit A).

Accordingly, Applicants respectfully submit that the pending claims meet the written description requirement under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that amended claims are fully enabled by and described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Enablement

Claims 1 to 23, 40, 41, 67 to 81 and 82 to 85 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. In particular, it is alleged that it would require undue experimentation for one skilled in the art to arrive at the genus of claimed nucleic acids.

The Patent Office state that the specification is enabling for an isolated nucleic acid encoding a polypeptide having phosphatase activity, wherein said polypeptide comprises SEQ ID NO:30.

However, it is alleged that the specification does not reasonable provide enablement for any nucleic acid or polynucleotide probe which is fully complementary to a portion of SEQ ID NO:21.

Applicants respectfully maintain that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, a genus of phosphatases to practice the claimed methods. The state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art, e.g., screening enzymes, and nucleic acids encoding enzymes, for phosphatase activity, was very high. Accordingly, it would not have taken undue experimentation to make and use the claimed invention, including identification of nucleic acids encoding phosphatases.

In fact, whether large numbers of compositions (e.g., enzymes, antibodies, nucleic acids, and the like) must be screened to determine if one is within the scope of the claimed invention is irrelevant to an enablement inquiry. Enablement is not precluded by the necessity to screen large numbers of compositions, as long as that screening is "routine," i.e., not "undue," to use the words of the Federal Circuit. As the Patent Office correctly notes, the Federal Circuit in In re Wands directed that the focus of the enablement inquiry should be whether the experimentation needed to practice the invention is or is not "undue" experimentation. The court set forth specific factors to be considered.

One of these factors is "the quantity of experimentation necessary." Guidance as to how much experimentation may be needed and still not be "undue" was set forth by the Federal Circuit in, e.g. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231

USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). In Hybritech, Inc., a single deposited antibody producing cell line enabled a claim generic to all IgM antibodies directed to a specific antigen. The Federal Circuit noted that the evidence indicated that those skilled in the monoclonal antibody art could, using the state of the art and applicants' written disclosure, produce and screen new hybridomas secreting other monoclonal antibodies falling within the genus without undue experimentation. The court held that applicants' claims need not be limited to the specific, single antibody secreted by the deposited hybridoma cell line (significantly, the genus of antibodies was allowed even though only one antibody specie was disclosed). The court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

Analogously, practitioners of the biological sciences for the instant invention also recognize the need to screen numbers of negatives to find a sample that has the desired properties, e.g., a phosphatase activity. Furthermore, the screening procedures used to identify nucleic acids within the scope of the instant invention (e.g., identifying phosphatase activity) were all well known in the art and at the time this application was filed. All were routine protocols for the skilled artisan. Thus, the skilled artisan using Applicants' written disclosure could practice the instant claimed invention without undue experimentation.

With the guidance provided in the specification it would only have required the skilled artisan routine experimentation to practice the full scope of the claimed invention. Accordingly, Applicants respectfully submit that the specification enables one of ordinary skill in the art to practice the full scope of the methods of the invention.

Issues under 35 U.S.C. §102

Claims 4 to 21, 67 to 70, 79 and 85 are rejected under 35 U.S.C. §102(e) for allegedly being anticipated by Hirschberg.

The legal standard for anticipation under 35 U.S.C. §102 is one of strict identity. To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention. In re Paulson, 30 F.3d 1475, 1478-79, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994)(citing In re Spada, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990)).

The Patent Office alleges that Hirschberg teaches a region from nucleotides 1551 to 1565 (15 nucleotides) that is 88.67% identical to SEQ ID NO:21 from nucleotides 337 to 351.

After entry of the instant amendment, the appropriate claims are directed to nucleic acids at least 20 residues in length. Accordingly, after entry of the instant amendment, because Hirschberg is not a single prior source that contains each and every limitation of the invention of claims 4 to 21, 67 to 70, 79 and 85, it cannot anticipate these claim.

CONCLUSION

In view of the foregoing amendment and remarks, it is believed that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs and 35 U.S.C. §102(e). Applicants believe all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050. Please credit any overpayment to this account.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (858) 678-5070.

Respectfully submitted,

Date: July 25, 2003

Gregory P. Einhorn
Reg. No. 38,440

Fish & Richardson P.C.
4350 La Jolla Village Drive, Suite 500
San Diego, California 92122
Telephone: (858) 678-5070
Facsimile: (858) 678-5099